OraPharma, Inc.	
Pharmaceutical Company	•
Minocycline Periodontal Therapeutic System	***
Investigating Product	
Multicenter Phase III Trial of Minocycline Periodontal Therapeutic System (Minocycline PTS): Adjunctive Use Patients with Adult Periodontitis (OPI-103A & B)	
Title of Study/Protocol #	
Dr. Ingvar Magnusson	ij
Investigator	7/

Yes No	Do you, your spouse or dependent children have a financial arrangen whereby the value of compensation to you, your spouse or dependent by the outcome of the study? This includes compensation that could clinical result, compensation in the form of an equity interest in Oral tied to sales of the product tested in the above study such as a royalty the financial arrangement is as follows:	t children could be influenced be grater for a favorable Pharma, Inc. or compensation
Yes No	Do you, your spouse or dependent children have a proprietary interest Therapeutic Systems (Minocycline MPTS) such as patent rights or trademark, copyright or licensing agreement? If yes, the nature of the follows:	rights under a patent, e proprietary interest is as
Yes No	Do you, your spouse or dependent children, or any of you combined interest in OraPharma, Inc. such as an ownership interest, stock opinterest whose value cannot be readily determined through reference in OraPharma, Inc. (if it is a publicly traded organization) exceeding of these? If yes, the amount and nature of the equity interest is as follows:	tions or any other financial to public prices, or any equity ng \$50,000, or any combination
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. such as an ownership interest, stock options or any value cannot be readily determined through reference to public price OraFharma, Inc. (if it is a publicly traded organization) exceeding these If yes, the amount and nature of the equity interest is as follows:	y other financial interest whose s, or any equity interest in \$50,000, or any combination of ws:
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. in excess of \$25,000, exclusive of the costs of corsuch as honoraria, a grant or grants to fund ongoing research, compe equipment, or retainers for ongoing consultation? If yes, the amount follows:	nducting the clinical studies, insation in the form of and nature of the payment is as
To the best of my knowledge, the information provided above is correct and complete. I understand that I am obligated to amend this statement and notify OraPharma, Inc. promptly if there is any change in this information during the conduct of the clinical studies listed above or during one year after the studies have been completed.		
ing		Sex 8 . 1999
	Signature of investigator	Pate

	OraPharma. Inc.	
	Pharmaceutical Company	
٠	Minocycline Periodontal Therapeutic System	_ 4
	Investigating Product	_
	Multicenter Phase III Trial of Minocycline Periodontal Therapeutic System (Minocycline PTS): Adjunctive Use in Patients with Adult Periodontitis (OPI-103A & B)	•
	Title of Study/Protocol #	
	Dr. Richard Oringer	7
	 Investigator	7
No.	, your spouse or dependent children have a financial arrangement y the value of compensation to you, your spouse or dependent chi	

Yes No	Do you, your spouse or dependent children have a financial arrangement whereby the value of compensation to you, your spouse or dependent by the outcome of the study? This includes compensation that could clinical result, compensation in the form of an equity interest in Oral tied to sales of the product tested in the above study such as a royalty the financial arrangement is as follows:	t children could be influenced be grater for a favorable Pharma, Inc. or compensation
Yes No	Do you, your spouse or dependent children have a proprietary interest Therapeutic Systems (Minocycline MPTS) such as patent rights or trademark, copyright or licensing agreement? If yes, the nature of the follows:	rights under a patent,
Yes Ng	Do you, your spouse or dependent children, or any of you combined interest in OraPharma, Inc. such as an ownership interest, stock opt interest whose value cannot be readily determined through reference in OraPharma, Inc. (if it is a publicly traded organization) exceeding of these? If yes, the amount and nature of the equity interest is as follows:	tions or any other financial to public prices, or any equity g \$50,000, or any combination
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. such as an ownership interest, stock options or any value cannot be readily determined through reference to public price. Orapharma, Inc. (if it is a publicly traded organization) exceeding these. If yes, the amount and nature of the equity interest is as follows:	y other financial interest whose s, or any equity interest in \$50,000, or any combination of
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. in excess of \$25,000, exclusive of the costs of consuch as honoraria, a grant or grants to fund ongoing research, comperequipment, or retainers for ongoing consultation? If yes, the amount follows:	nducting the clinical studies, insation in the form of and nature of the payment is as
notify OraPharma, Incafter the studies have be	c. promptly if there is any change in this information during the conduct of the clinical s	tudies listed above or during one year
Pelli O		9-7-99
	Signature of Investigator	Date

OraPharma, Inc.	
Pharmaceutical Company	
Minocycline Periodontal Therapeutic System	
Investigating Product	
Multicenter Phase III Trial of Minocycline Periodo	ntal
Therapeutic System (Minocycline PTS): Adjunctive \	Ise in
Therapeutic System (Minocycline PTS): Adjunctive & Patients with Adult Periodontitis (OPI-103A & B	
Patients with Adult Periodontitis (OPI-103A & B	

Yes No	Do you, your spouse or dependent children have a financial arrangement whereby the value of compensation to you, your spouse or dependent by the outcome of the study? This includes compensation that could climical result, compensation in the form of an equity interest in Oral tied to sales of the product tested in the above study such as a royalty the financial arrangement is as follows:	t children could be influenced be grater for a favorable Pharma, Inc. or compensation interest. If yes, the nature of
Yes No	Do you, your spouse or dependent children have a proprietary interest.  Therapeutic Systems (Minocycline MPTS) such as patent rights or trademark, copyright or licensing agreement? If yes, the nature of the follows:	rights under a patent,
Yes No	Do you, your spouse or dependent children, or any of you combined interest in OraPharma, Inc. such as an ownership interest, stock op interest whose value cannot be readily determined through reference in OraPharma, Inc. (if it is a publicly traded organization) exceeding of these? If yes, the amount and nature of the equity interest is as for	tions or any other financial to public prices, or any equity ng \$50,000, or any combination
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. such as an ownership interest, stock options or an value cannot be readily determined through reference to public price Orapharma, Inc. (if it is a publicly traded organization) exceeding these. If yes, the amount and nature of the equity interest is as follows:	y other financial interest whose s, or any equity interest in \$50,000, or any combination of ws:
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. in excess of \$25,000, exclusive of the costs of corsuch as honoraria, a grant or grants to fund ongoing research, competed equipment, or retainers for ongoing consultation? If yes, the amount follows:	nducting the clinical studies, ensation in the form of t and nature of the payment is as
notify OraPharm	Line-promptly if there is any change in this information during the conduct of the clinical second configuration.	studies listed above or during one year
1	to occur constraint.	9-21-66
JIMA	~ Ymn	
V	Signature of Investigator	alk '

OraPharma, Inc.	· · · · · · · · · · · · · · · · · · ·
Pharmaceutical Company	
Minocycline Periodontal Therapeutic Sy	rstem
Investigating Product	
Multicenter Phase III Trial of Minocycline Po Therapeutic System (Minocycline PTS): Adjun Patients with Adult Periodontitis (OPI-103	ctive Use in
Title of Study/Protocol #	
Dr. Donald Adams	Ÿ
Investigator	···

	٠	
Yes No DX	Do you, your spouse or dependent children have a financial arrangen whereby the value of compensation to you, your spouse or dependent by the outcome of the study? This includes compensation that could chinical result, compensation in the form of an equity interest in Oral tied to sales of the product tested in the above study such as a royalty the financial arrangement is as follows:	t children could be influenced be grater for a favorable Pharma, Inc. or compensation
Yes No □ <b>E</b> I	Do you, your spouse or dependent children have a proprietary interest. Therapeutic Systems (Minocycline MPTS) such as patent rights or trademark, copyright or licensing agreement? If yes, the nature of the follows:	rights under a patent,
Yes No	Do you, your spouse or dependent children, or any of you combined interest in OraPharma, Inc. such as an ownership interest, stock opinterest whose value cannot be readily determined through reference in OraPharma, Inc. (if it is a publicly traded organization) exceeding of these? If yes, the amount and nature of the equity interest is as follows:	tions or any other financial to public prices, or any equity ig \$50,000, or any combination
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. such as an ownership interest, stock options or any value cannot be readily determined through reference to public price OraPharma, Inc. (if it is a publicly traded organization) exceeding these. If yes, the amount and nature of the equity interest is as follows:	y other financial interest whose s, or any equity interest in \$50,000, or any combination of
Yes No Da V.	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. in excess of \$25,000, exclusive of the costs of corsuch as honoraria, a grant or grants to fund ongoing research, compe equipment, or retainers for ongoing consultation? If yes, the amount follows:	nducting the clinical studies, nsation in the form of and nature of the payment is as
To the best of my know notify OraPharma, In after the studies have be	ledge, the information provided above is correct and complete. I understand that I am on promptly if there is any change in this information during the conduct of the clinical seen completed.	bligated to amend this statement and tudies listed above or during one year
	Durid Heten	Sept 14, 1999
	Signature of Investigator	Pate

OraPharma, Inc.	
Pharmaceutical Company	_
Minocycline Periodontal Therapeutic System	··
Investigating Product	
Multicenter Phase III Trial of Minocycline Periodontal Therapeutic System (Minocycline PTS): Adjunctive Use in Patients with Adult Periodontitis (OPI-103A & B)	,
Title of Study/Protocol #	
Dr. Connie Drisko	,
Investigator	_

Yes No	Do you, your spouse or dependent children have a financial arrangen whereby the value of compensation to you, your spouse or dependent by the outcome of the study? This includes compensation that could clinical result, compensation in the form of an equity interest in Oral tied to sales of the product tested in the above study such as a royalty the financial arrangement is as follows:	t children could be influenced be grater for a favorable Pharma, Inc. or compensation
Yes No □ K	Do you, your spouse or dependent children have a proprietary interest Therapeutic Systems (Minocycline MPTS) such as patent rights or trademark, copyright or licensing agreement? If yes, the nature of the follows:	rights under a patent, e proprietary interest is as
Yes No	Do you, your spouse or dependent children, or any of you combined interest in OraPharma, Inc. such as an ownership interest, stock opinterest whose value cannot be readily determined through reference in OraPharma, Inc. (if it is a publicly traded organization) exceeding of these? If yes, the amount and nature of the equity interest is as follows:	tions or any other financial to public prices, or any equity ag \$50,000, or any combination
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. such as an ownership interest, stock options or any value cannot be readily determined through reference to public price Ora harma, Inc. (if it is a publicly traded organization) exceeding these. If yes, the amount and nature of the equity interest is as follows:	y other financial interest whose s, or any equity interest in \$50,000, or any combination of ws:
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. in excess of \$25,000, exclusive of the costs of consuch as honoraria, a grant or grants to fund ongoing research, competequipment, or retainers for ongoing consultation? If yes, the amount follows:	nducting the clinical studies, insation in the form of and nature of the payment is as obligated to amend this statement and
notify OraPharma, Inc. promptly if there is any change in this information during the conduct of the clinical studies listed above or during one year after the studies have been completed.		
	Ami blu	9-9-99
	Signature of Investigator	w

OraPharma, Inc.	•
Pharmaceutical Company	
Minocycline Periodontal Therapeutic S	ystem
Investigating Product	-
Multicenter Phase III Trial of Minocycline P	
Therapeutic System (Minocycline PTS): Adjur	ictive Use in
Patients with Adult Periodontitis (OPI-103	(A & B)
Title of Study/Protocol #	
Dr. Robert Genco	
Dr. Robert Genco Investigator	·

F=	<u> </u>	
Yes	Do you, your spouse or dependent children have a financial arranger whereby the value of compensation to you, your spouse or dependent by the outcome of the study? This includes compensation that could chinical result, compensation in the form of an equity interest in Oral tied to sales of the product tested in the above study such as a royalty the financial arrangement is as follows:	at children could be influenced i be grater for a favorable Pharma, Inc. or compensation
Yes No	Do you, your spouse or dependent children have a proprietary intere Therapeutic Systems (Minocycline MPTS) such as patent rights or trademark, copyright or licensing agreement? If yes, the nature of the follows:	r rights under a patent,
Yes Ng	Do you, your spouse or dependent children, or any of you combined interest in OraPharma, Inc. such as an ownership interest, stock op interest whose value cannot be readily determined through reference in OraPharma, Inc. (if it is a publicly traded organization) exceeding of these? If yes, the amount and nature of the equity interest is as for	etions or any other financial to public prices, or any equity ng \$50,000, or any combination
Yes No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. such as an ownership interest, stock options or an value cannot be readily determined through reference to public price OraPharma, Inc. (if it is a publicly traded organization) exceeding these. If yes, the amount and nature of the equity interest is as follows:	sy other financial interest whose es, or any equity interest in \$50,000, or any combination of ws:
Yes No	Have you, your spouse or dependent children, or any of you combin OraPharma, Inc. in excess of \$25,000, exclusive of the costs of costs as honoraria, a grant or grants to fund ongoing research, compe equipment, or retainers for ongoing consultation? If yes, the amount follows:	nducting the clinical studies, ensation in the form of t and nature of the payment is as
To the best of my know notify OraPharma. In	riedge, the information provided above is correct and complete. I understand that I am on the promptly of there is any change in this information during the conduct of the clinical a	obligated to amend this statement and studies listed, above or during one year
after the studies have b	een completed.	a/0/c/1.
	11/1/1/	7/04/14
	// / Signature of Investigator	Date

This information below is provided in accordance with 21 CFR Part 54 in regard to the following clinical study.

OraPharma, Inc.
Pharmaceutical Company

		Minocycline Periodontal Therapeutic System
		Investigating Product
		Multicenter Phase III Trial of Minocycline Periodontal
		Therapeutic System (Minocycline PTS): Adjunctive Use in
		Patients with Adult Periodontitis (OPI-103A & B)
		Title of Study/Protocol #
		· ·
		Dr. John Rapley
		Investigator
Yes	No/	Do you, your spouse or dependent children have a financial arrangement with OraPharma, Inc.,
	H H	whereby the value of compensation to you, your spouse or dependent children could be influenced
_		by the outcome of the study? This includes compensation that could be grater for a favorable
	E	clinical result, compensation in the form of an equity interest in OraPharma, Inc. or compensation
	ı	tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of
		the financial arrangement is as follows:
Yes	No	Do you, your spouse or dependent children have a proprietary interest in Minocycline Periodontal
	X	Therapeutic Systems (Minocycline MPTS) such as patent rights or rights under a patent,
		trademark, copyright or licensing agreement? If yes, the nature of the proprietary interest is as
		follows:
	/ · · · · · · · · · · · · · · · · · · ·	
	<del></del>	
Yes	(Ng	Do you, your spouse or dependent children, or any of you combined have a significant equity
	<b>X</b>	interest in OraPharma, Inc. such as an ownership interest, stock options or any other financial
		interest whose value cannot be readily determined through reference to public prices, or any equity in OraPharma, Inc. (if it is a publicly traded organization) exceeding \$50,000, or any combination
		of these? If yes, the amount and nature of the equity interest is as follows:
		of these: If yes, the amount and nature of the equity microst is as follows.
	, \	•
Yes	(No)	Have you, your spouse or dependent children, or any of you combined received payments from
	· 6	OraPharma, Inc. such as an ownership interest, stock options or any other financial interest whose
		value cannot be readily determined through reference to public prices, or any equity interest in
	~	Oral harma, Inc. (if it is a publicly traded organization) exceeding \$50,000, or any combination of
		these. If yes, the amount and nature of the equity interest is as follows:
•		
		· ·
Yes	\ Nø	Have you, your spouse or dependent children, or any of you combined received payments from
	X	OraPharma, Inc. in excess of \$25,000, exclusive of the costs of conducting the clinical studies,
		such as honoraria, a grant or grants to fund ongoing research, compensation in the form of
	ξ.	equipment, or retainers for ongoing consultation? If yes, the amount and nature of the payment is as
•	· V	follows:
To the b	et of any langue	ledge, the information provided above is correct and complete. I understand that I am obligated to amend this statement and
notify O	raPharma. In:	c. promptly is there is any change in this information during the conduct of the clinical studies listed above or during one year
after the	studies have be	en completed.

Signature of Investiga

OraPharma, Inc.	•
Pharmaceutical Company	***
Minocycline Periodontal Therapeutic Sy	ystem
Investigating Product	
Multicenter Phase III Trial of Minocycline P Therapeutic System (Minocycline PTS): Adjur Patients with Adult Periodontitis (OPI-103	nctive Use in
Title of Study/Protocol #	
Dr. Ira Lamster	
Investigator	•

Yes	No	Do you, your spouse or dependent children have a financial arrangement with OraPharma, Inc., whereby the value of compensation to you, your spouse or dependent children could be influenced by the outcome of the study? This includes compensation that could be grater for a favorable clinical result, compensation in the form of an equity interest in OraPharma, Inc. or compensation tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of the financial arrangement is as follows:		
Yes	No M	Do you, your spouse or dependent children have a proprietary interest in Minocycline Periodontal Therapeutic Systems (Minocycline MPTS) such as patent rights or rights under a patent, trademark, copyright or licensing agreement? If yes, the nature of the proprietary interest is as follows:		
Yes	No.	Do you, your spouse or dependent children, or any of you combined have a significant equity interest in OraPharma, Inc. such as an ownership interest, stock options or any other financial interest whose value cannot be readily determined through reference to public prices, or any equity in OraPharma, Inc. (if it is a publicly traded organization) exceeding \$50,000, or any combination of these? If yes, the amount and nature of the equity interest is as follows:		
Yes	No V	Have you, your spouse or dependent children, or any of you combined received payments from OraPharma, Inc. such as an ownership interest, stock options or any other financial interest whose value cannot be readily determined through reference to public prices, or any equity interest in Orapharma, Inc. (if it is a publicly traded organization) exceeding \$50,000, or any combination of these If yes, the amount and nature of the equity interest is as follows:		
Yes				
notify C	est of my know braPharma, Inc studies have be	edge, the information provided above is correct and complete. I understand that I am obligated to amend this statement and promptly if there is any change in this information during the conduct of the clinical studies listed above or during one year en completed.		
		Signature of Investigator		

OraPharma, Inc.	
Pharmaceutical Company	_
Minocycline Periodontal Therapeutic System	
Investigating Product	_
Multicenter Phase III Trial of Minocycline Periodontal Therapeutic System (Minocycline PTS): Adjunctive Use in	
Patients with Adult Periodontitis (OPI-103A & B)	
Title of Study/Protocol #	
Dr. David Paquette	i
	_
Investigator	٠,

			•
Yes	No E	Do you, your spouse or dependent children have a financial arrangem whereby the value of compensation to you, your spouse or dependent by control of the study? This includes compensation that could climical result, compensation in the form of an equity interest in Oral tied to sales of the product tested in the above study such as a royalty the financial arrangement is as follows:	children could be influenced be grater for a favorable Pharma, Inc. or compensation
Yes	No D	Do you, your spouse or dependent children have a proprietary interes Therapeutic Systems (Minocycline MPTS) such as patent rights or trademark, copyright or licensing agreement? If yes, the nature of the follows:	rights under a patent, e proprietary interest is as
Yes	No	Do you, your spouse or dependent children, or any of you combined interest in OraPharma, Inc. such as an ownership interest, stock opt interest whose value cannot be readily determined through reference in OraPharma, Inc. (if it is a publicly traded organization) exceedin of these? If yes, the amount and nature of the equity interest is as follows:	ions or any other financial to public prices, or any equity g \$50,000, or any combination
Yes	No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. such as an ownership interest, stock options or any value cannot be readily determined through reference to public prices Oracharma, Inc. (if it is a publicly traded organization) exceeding these. If yes, the amount and nature of the equity interest is as follows:	y other financial interest whose s, or any equity interest in \$50,000, or any combination of
Yes	No	Have you, your spouse or dependent children, or any of you combine OraPharma, Inc. in excess of \$25,000, exclusive of the costs of con such as honoraria, a grant or grants to fund ongoing research, comper equipment, or retainers for ongoing consultation? If yes, the amount follows:	ducting the clinical studies, nsation in the form of and nature of the payment is as
notify OraF	barma, In	viedge, the information provided above is correct and complete. I understand that I am of e. promptly if there is any change in this information during the conduct of the clinical steen completed.	bligated to amend this statement and tudies listed above or during one year
Dur	5	Signature of Investigator	11 Nov. 1229
			•

OraPharma, Inc.	
Pharmaceutical Company	
Minocycline Periodontal Therapeutic System	-
Investigating Product	_
Multicenter Phase III Trial of Minocycline Periodontal Therapeutic System (Minocycline PTS): Adjunctive Use in Patients with Adult Periodontitis (OPI-103A & B)	1. 
Title of Study/Protocol #	-
Dr. Sigmund Socransky	
Investigator	<del>-</del>

Yes No	Do you, your spouse or dependent children have a financial arrangen whereby the value of compensation to you, your spouse or dependent by the outcome of the study? This includes compensation that could clinical result, compensation in the form of an equity interest in Oral tied to sales of the product tested in the above study such as a royalty the financial arrangement is as follows:	t children could be influenced be grater for a favorable Pharma, Inc. or compensation interest. If yes, the nature of		
Yes No □ Æ	Do you, your spouse or dependent children have a proprietary interest. Therapeutic Systems (Minocycline MPTS) such as patent rights or trademark, copyright or licensing agreement? If yes, the nature of the follows:	rights under a patent, e proprietary interest is as		
Yes No	Do you, your spouse or dependent children, or any of you combined interest in OraPharma, Inc. such as an ownership interest, stock op interest whose value cannot be readily determined through reference in OraPharma, Inc. (if it is a publicly traded organization) exceeding of these? If yes, the amount and nature of the equity interest is as follows:	tions or any other financial to public prices, or any equity ag \$50,000, or any combination		
Yes No BO	Have you, your spouse or dependent children, or any of you combined received payments from OraPharma, Inc. such as an ownership interest, stock options or any other financial interest whose value cannot be readily determined through reference to public prices, or any equity interest in Ora harma, Inc. (if it is a publicly traded organization) exceeding \$50,000, or any combination of these. If yes, the amount and nature of the equity interest is as follows:			
Have you, your spouse or dependent children, or any of you combined received payments from  OraPharma, Inc. in excess of \$25,000, exclusive of the costs of conducting the clinical studies, such as honoraria, a grant or grants to fund ongoing research, compensation in the form of equipment, or retainers for ongoing consultation? If yes, the amount and nature of the payment is as follows:  To the best of my knowledge, the information provided above is correct and complete. I understand that I am obligated to amend this statement and				
notify OraPharma, Inc. promptly if there is any change in this information during the conduct of the clinical studies listed above or during one year after the studies have been completed.				
Signish & Socransky - 09/07/1999				
	Signature of Investigator// Date			

OraPharma, Inc.	
Pharmaceutical Company	_
Minocycline Periodontal Therapeutic System	-
Investigating Product	
Multicenter Phase III Trial of Minocycline Periodontal Therapeutic System (Minocycline PTS): Adjunctive Use in Patients with Adult Periodontitis (OPI-103A & B)	
Title of Study/Protocol #	-
Dr. Thomas Van Dyke	
Investigator	7

		· · · · · · · · · · · · · · · · · · ·
Yes	No 🔁	Do you, your spouse or dependent children have a financial arrangement with OraPharma, Inc., whereby the value of compensation to you, your spouse or dependent children could be influenced by the outcome of the study? This includes compensation that could be grater for a favorable clinical result, compensation in the form of an equity interest in OraPharma, Inc. or compensation tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of the financial arrangement is as follows:
Yes	No	Do you, your spouse or dependent children have a proprietary interest in Minocycline Periodontal Therapeutic Systems (Minocycline MPTS) such as patent rights or rights under a patent, trademark, copyright or licensing agreement? If yes, the nature of the proprietary interest is as follows:
Yes	No 🔽	Do you, your spouse or dependent children, or any of you combined have a significant equity interest in OraPharma, Inc. such as an ownership interest, stock options or any other financial interest whose value cannot be readily determined through reference to public prices, or any equity in OraPharma, Inc. (if it is a publicly traded organization) exceeding \$50,000, or any combination of these? If yes, the amount and nature of the equity interest is as follows:
Yes	No 🖼	Have you, your spouse or dependent children, or any of you combined received payments from OraPharma, Inc. such as an ownership interest, stock options or any other financial interest whose value cannot be readily determined through reference to public prices, or any equity interest in Oral harma, Inc. (if it is a publicly traded organization) exceeding \$50,000, or any combination of these If yes, the amount and nature of the equity interest is as follows:
Yes No Dalla Have you, your spouse or dependent children, or any of you combined received payments from OraPharma, Inc. in excess of \$25,000, exclusive of the costs of conducting the clinical studies, such as honoraria, a grant or grants to fund ongoing research, compensation in the form of equipment, or retainers for ongoing consultation? If yes, the amount and nature of the payment is as follows:		
To the best of notify OraP after the stu	of my know harma, kn dies have b	viedge, the information provided above is correct and complete. I understand that I am obligated to amend this statement and promptly if there is any change in this information during the conduct of the clinical studies listed above or during one year een completed.
	مروح	Signature of Investigator  Signature of Investigator
L		

		Clinical Investigator Financial Certification
	This inform	nation below is provided in accordance with 21 CFR Part 54 in regard to the following clinical study.
		OraPharma, Inc.
		Pharmaceutical Company
		Minocycline Periodontal Therapeutic System
		Investigating Product
		Multicenter Phase III Trial of Minocycline Periodontal
		Therapeutic System (Minocycline PTS): Adjunctive Use in
		Patients with Adult Periodontitis (OPI-103A & B)
		Title of Study/Protocol #
		<b>4</b>
		Dr. Larry Wolff
		Investigator
Yes	No	Do you, your spouse or dependent children have a financial arrangement with OraPharma, Inc.,
	¥	whereby the value of compensation to you, your spouse or dependent children could be influenced
_	ア	by the outcome of the study? This includes compensation that could be grater for a favorable
	· 4	clinical result, compensation in the form of an equity interest in OraPharma, Inc. or compensation
		tied to sales of the product tested in the above study such as a royalty interest. If yes, the nature of
		the financial arrangement is as follows:
		•
Yes	No	Do you, your spouse or dependent children have a proprietary interest in Minocycline Periodontal
	R	Therapeutic Systems (Minocycline MPTS) such as patent rights or rights under a patent,
		trademark, copyright or licensing agreement? If yes, the nature of the proprietary interest is as follows:
		Tonows.
		·
Yes	No	Do you, your spouse or dependent children, or any of you combined have a significant equity
	À	interest in OraPharma, Inc. such as an ownership interest, stock options or any other financial
	•	interest whose value cannot be readily determined through reference to public prices, or any equity
		in OraPharma, Inc. (if it is a publicly traded organization) exceeding \$50,000, or any combination
		of these? If yes, the amount and nature of the equity interest is as follows:
Yes	_No	Have you, your spouse or dependent children, or any of you combined received payments from
	<b>X</b>	OraPharma, Inc. such as an ownership interest, stock options or any other financial interest whose
_	7	value cannot be readily determined through reference to public prices, or any equity interest in
		Oral narma, Inc. (if it is a publicly traded organization) exceeding \$50,000, or any combination of
		there. If yes, the amount and nature of the equity interest is as follows:
Yes	No	Have you, your spouse or dependent children, or any of you combined received payments from
	À	OraPharma, Inc. in excess of \$25,000, exclusive of the costs of conducting the clinical studies,
		such as honoraria, a grant or grants to fund ongoing research, compensation in the form of equipment, or retainers for ongoing consultation? If yes, the amount and nature of the payment is as
		edinhument or teramers for outloung comparisation: it has me amount and nature of the balancing is as

To the best of my knowledge, the information provided above is correct and complete. I understand that I am obligated to amend this statement and notify OraPharma. Inc. promptly if there is any change in this information during the conduct of the clinical studies listed above or during one year after the studies have been completed.

sature of Investigator

follows:

### Correspondence from Applicant

01-30-01

raPharma, Inc.

www.orapharma.com

732 Louis Drive Warminster, PA 18974

> 215/956-2200 Tel 215/443-9531 Fax

January 30, 2001

Jonathan K. Wilkin, MD
Director, Division of Dermatological and Dental Drug Products (HFD-540)
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

B--

RE: NDA 50-781

Arestin (minocycline hcl) microspheres, 1mg Amendment Correction to NDA Amendment 24.1, 24.2

Dear Dr. Wilkin:

Reference is made to OraPharma, Inc.'s submission of January 25, 2001 Amendment #24.1 and 24.2.

During our QA check of the submission the following typographical error was detected in volume 24.2.

In our haste to submit the requested CMC information by the timeframe given, under point 2, appendix #2, Table 1, we inadvertently referenced filling machine as

Attached is the corrected table with the correction in bold. Please replace the table in Volume 24.2 in the original and archival copies.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

Markus F. Herzig

Executive Director, Regulatory Affairs and Quality Assurance

Form FDA.356h Submitted in duplicate Desk copy to K. Bhatt

DUFLICATE

### Correspondence from Applicant 1-25-01



www.orapharma.com

732 Louis Drive Warminster, PA 18974

> 215/956-2200 Tel 215 443-9531 Fax

January 25, 2001

Jonathan K. Wilkin, MD Director, Division of Dermatological and Dental Drug Products (HFD-540); Center for Drug Evaluation & Research Food and Drug Administration **Document Control Room** 9201 Corporate Boulevard Rockville, MD 20850

RE:

NDA 50-781

Arestin (minocycline hcl) microspheres, 1mg

Amendment: No. 24.1, FDA Requested CMC Information

Dear Dr. Wilkin:

Reference is made to a teleconference between Drs. DeCamp and Gautam-Basak and Ms. K. Bhatt in your Division and Dr. Lawter and Mr. Herzig of OraPharma, Inc. on December 19, 2000. During this teleconference Dr. DeCamp identified a number of issues OraPharma needed to address. The teleconference was followed up by a telefax dated December 22, 2000 which provided the items in writing.

Attached/enclosed are OraPharma, Inc.'s responses to these items. For completeness, I restated the FDAs requests followed by our responses. For item 3 we have enclosed a dispenser/cartridge handle and a pouch containing 12 filled unit dose cartridges in the desk copy package address to Ms. K. Bhatt.

As I indicated in my telefax copy of January 24, 2001, regarding the particle size specifications for the bulk microspheres, this information is included in this amendment submission as the last tab in volume 2.

If you have an questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

Executive Director, Regulatory Affairs and Quality Assurance

Form FDA 356h

Submitted in duplicate

Desk copy to K. Bhatt

(containing the dispenser handle and a 12 cartridge pouch of drug

product)

# ince the Content of t

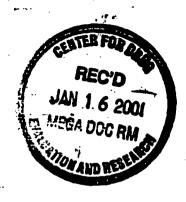






www.orapharma.com

January 12, 2001



732 Lo Warminster,

> 215/956-215/443-1

Jonathan K. Wilkin, MD

Director, Division of Dermatological and Dental Drug Products (HFD-540)

Center for Drug Evaluation & Research

Food and Drug Administration

Document Control Room

9201 Corporate Boulevard

NDA ORIG AMENDMENT

SU

RE: NDA 50-781

Rockville, MD 20850

Arestin (minocycline hcl) microspheres, 1mg Amendment: Clinical – Final Safety Update

Dear Dr. Wilkin:

Reference is made to a telephone call on January 11, 2001 between Ms. K. Bhatt in your Division and the undersigned. Ms. Bhatt requested OraPharma, Inc. to provide a final safety update for the above referenced NDA.

Attachment 1 summarized the clinical safety since our 120-day safety update submission of June 16, 2000 (amendment 4.1 – 4.14). As the summary shows there were no additional safety reports to submit, as no studies were ongoing until the start-up recently of some pilot-studies.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

Markus F. Herzig

Executive Director, Regulatory Affairs and Quality Assurance

Form FDA 356h Submitted in duplicate

### 

### PHARMA, INC.

ww.orapharma.com



215/956-2200 Tel

NDW ONE AMENDMENT

BC

215/443-9531 Fax

132 Louis Drive Warminster, PA 18974

January 10, 2001

Ionathan K. Wilkin, MD

Director, Division of Dermatological and Dental Drug Products (HFD-540)

Center for Drug Evaluation & Research

Food and Drug Administration

Document Control Room

9201 Corporate Boulevard

Rockville, MD 20850

RE:

NDA 50-781

Arestin (minocycline hcl) microspheres, 1mg

Amendment: CMC Amendment

Dear Dr. Wilkin:

This CMC amendment contains updated dispenser (cartridge) components specifications and test methods (STM). These revisions were made to reflect commercial production of these components. At the same time, typographical errors were also corrected.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

Markus F. Herzia /

Executive Director, Regulatory Affairs and Quality Assurance

Form FDA 356h

Submitted in duplicate

ORIGINAL

## 



215/956-2200 Tel 215/443-9531 Fax

January 9, 2001

NDA ORIG HAENDMENT

XR

Jonathan K. Wilkin, MD

Director, Division of Dermatological and Dental Drug Products (HFD-540)

Center for Drug Evaluation & Research

Food and Drug Administration

**Document Control Room** 

9201 Corporate Boulevard

Rockville, MD 20850

RE:

NDA 50-781

Arestin (minocycline hcl) microspheres, 1mg

Amendment: Marketing Exclusivity

Dear Dr. Wilkin:

Reference is made to a telephone call on January 9, 2001 by Ms. K. Bhatt in your Division with the undersigned in which she requested OraPharma, Inc. to officially request marketing exclusivity for the above referenced product according to the patents covering this product.

OraPharma, Inc. herewith requests market exclusivity until August 17, 2010 for Arestin™. August 17, 2010 is the date when the latest two patents (patent no. 5236355 and patent no. 5622498) expire.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

I also attached a copy of the cover letter dated June 5, 2000 (amendment 3.1) in which OraPharma, Inc. provided microbiology feedback to questions raised by Dr. Riley, for which we would appreciate receiving feedback as we have worked on finding a more sensitive method to measure bioburden.

Sincerely.

Markus F. Herzig

Executive Director; Regulatory Affairs and Quality Assurance

Form FDA 356h

Submitted in duplicate

URIGINAL

## 

you have any questions regarding this submission, please contact me at (215) 956-207.

ncerely,

arkus F. Herzig / xecutive Director, Regulatory Affairs and Quality Assurance

om FDA 356h submitted in duplicate

### Correspondence from Applicant 2-7-90

www.orapharma.com

732 Louis Drive Warminster, PA 18974

> 215/956-2200 Tel 215/443-9531 Fax

December 7, 2000

Jonathan K. Wilkin, MD
Director, Division of Dermatological and Dental Drug Products (HFD-540)
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
9201 Corporate Boulevard
Rockville, MD-20850

RE: NDA 50-781

Arestin (minocycline hcl) microspheres, 1mg

Amendment: Labeling

Dear Dr. Wilkin:

Reference is made to our draft package insert submitted in our original NDA on February 17, 2000 and our revision to your first draft submitted on December 1, 2000.

Reference is also made to a telephone conversation on December 6, 2000, with Ms. K. Bhatt from your Division and the undersigned. Ms. Bhatt informed OraPharma that our request to change the product unit dose referenced to in earlier correspondence as "tips" or "dispensers" to "cartridge(s)" is acceptable.

As requested, we have made the changes throughout the 2<sup>nd</sup> FDA draft label which OraPharma received via fax on December 5, 2000.

In table 4, we have identified a discrepancy which we could not verify. In the 5 mm data of Study OPI=103B your table lists the change as -1.32 mm. Our data shows that number as -1.63 mm. We note that Table 4 now presents PD changes based on varying depths in mm rather than percentages, and as study subgroups. We prefer this presentation, but since it is presented as study subgroups (at least for baseline PD  $\geq$  6 mm and  $\geq$  7 mm) we suggest it might be prudent to combine these data (see following table). This would make the data presentation more consistent with Table 3.

Table 4: Mean Pocket Depth Change in Patients with Mean Baseline PD ≥ 5 mm,
 ≥ 6 mm and ≥ 7 mm at 9 Months from Two Multicenter U.S. Clinical Trials

Mean Baseline Pocket Depth	SRP Alone	SRP + Vehicle	SRE+ ARESTINIM
≥ 5 mm at Baseline			7
≥ 6 mm at Baseline	<u> </u>	<del>-</del> -	<del>                                     </del>
			<u> </u>
≥ 7 mm at Baseline			

\*Statistically significant comparison between SRP + ARESTIN M and SRP alone

OraPharma, Inc. would like to express our appreciation for the work your Division executed in the revised drafting of the package insert.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

Markus F. Herzig

Executive Director, Regulatory Affairs and Quality Assurance

Form FDA 356h Submitted in duplicate OraPharma, Inc. 732 Louis Drive Warminster, PA 18974 215-956-2200 Facsimile: 215-443-9531



**FAX COVER SHEET** 

To:	Ms. Kalyani Bhatt, Project Manager	From: Markus Herzig
Company:	FDA	Date: December 7, 2000
Fax No.:	301-827-2075	No. of pages w/cover: 1
RE:	NDA-50-781	
X Urgent	Reply ASAP Please comment P	lease review For your information

Dear Ms. Bhatt:

As requested, attached is the revised draft package insert regarding the change from "tips" and" dispenser" to "cartridges".

We have identified a discrepancy in Table 4 and request corrections. Additionally, we propose a different presentation of Table 4.

If you have any questions, please don't hesitate to contact me.

Sincerely,

Markus F. Herzig

Executive Prector Regulatory Affairs and Quality Assurance

This facsimile contains confidential information intended for the person(s) named above. If you have received this facsimile in error, please notify us immediately by telephone and destroy this transmission.

No.9903 P. 1/11

Dec. 7. 2000 2:42PM